Material and Methods

Study Population

The HCHS/SOL is a community based cohort study consisting of 16,415 self-identified Hispanic/Latino participants aged 18 to 74 years residing in four U. S. urban areas (Bronx, NY; Chicago, IL; Miami, FL; San Diego, CA). The details of the study design, sampling strategy, and recruitment are described elsewhere.[1,2] In brief, all participants underwent a baseline interview and an extensive clinic examination (2008-2011) that included, but was not limited to, anthropometry, electrocardiogram (ECG), blood pressures in both arms, phlebotomy, glucose tolerance testing, audiometry, lung function tests and oral examinations. Questionnaires included sociodemographics, health and medical history, smoking, alcohol, occupational history and physical activity. Medication use was ascertained by MDDB (Medi-Span Master Drug Data base) Product line Therapeutic Classification System and also by directed questions about specific types of medications.

Individuals younger than 45 years of age (n=6,710) were excluded from this study, as they did not undergo ankle brachial index measurement. Individuals with ABI values >1.4 in either leg (n=189) were excluded as these individuals are considered to have stiff arteries likely due to medial artery sclerosis which may result in an artificially elevated ABI value.[3] Sleep studies with fewer than 30 minutes defined as incomplete (n=1,110) were excluded from all analyses. These non-exclusive criteria resulted in an analytic sample size of 8,367 participants.

Assessment of Ankle Brachial Index

Ankle brachial index measurements were obtained for all HCHS/SOL participants aged 45-74 years. Briefly, after resting quietly for 5 minutes, a Doppler probe was used to obtain systolic blood pressures (SBP) in the following order: right brachial artery, right dorsalis pedis artery, right posterior tibial artery, left posterior tibial artery, left dorsalis pedis artery and left brachial artery. Two separate ABIs were generated, one for each leg. The denominator for both ABIs was the highest SBP from either the left or right brachial artery. For each leg, the numerator was the higher of the two lower extremity measurements, i.e. posterior tibial SBP or dorsalis pedis SBP. PAD was defined as ABI < 0.9 in either leg.

Assessment of Sleep Symptoms and Sleep Apnea

Both subjective (questionnaire) and objective (overnight home study) sleep data were collected. The sleep questionnaire (interview-administered by study staff) included the Sleep Heart Health Study Sleep Habits questionnaire[4] to assess symptoms of SA and sleep patterns, and the Epworth Sleepiness Scale to assess daytime sleepiness.[5] Objective sleep apnea testing included measurement of overnight oxygen saturation (using a transcutaneous oximeter), airflow (using nasal cannula and pressure transducer), snoring sounds (by microphone) and head position and movement (ARES Unicorder 5.2; B-Alert, Carlsbad, CA).[6] Each participant underwent a self-administered test at home after receiving, during the baseline clinic visit, in-person demonstration and instruction on the application of the monitor. Sleep monitor data were scored by a central Sleep Reading Center (Case Western Reserve University/Brigham and Women's Hospital). Respiratory events were defined as a 50% or more reduction in airflow lasting at least 10 seconds. Apneas were not distinguished from hypopneas as thermistry was not available. Each respiratory event was manually identified and linked to its level of desaturation, and artifact was manually edited on an epoch-by-epoch basis. The current analyses used the 3% desaturation variable in accordance with current recommended

scoring criteria from the American Academy of Sleep Medicine.[7,8] The majority of the sleep studies (over 80%) included in the analyses had at least 4 hours of total recording time. The AHI obtained from the monitoring device has been shown to have excellent correlation with AHI obtained from in-lab attended sleep testing.[6,9] Clinically significant SA was defined as an AHI ≥15 per hour (associated with a 3% desaturation). Mild SA was defined as an AHI ≥ 5 and < 15, moderate SA as AHI ≥ 15 and < 30, and severe SA as AHI ≥ 30/hr. Inter- and–intra scorer reliability estimates for the AHI, assessed over the course of the study, were excellent (intraclass correlation coefficients > 0.99).

Covariates

Obesity was defined based on measured weight and height as a body-mass index (BMI) ≥ 30 kg/m^2. Waist and hip were measured and used to compute the waist-to-hip ratio, which was used as a marker of central adiposity. Hypertension was defined using recommendations from the Joint National Committee-7[10] as a blood pressure ≥140/90 mm Hg or a medication review revealing use of antihypertensive. Diabetes was defined according to recommendations from the American Diabetes Association[11] as a fasting glucose ≥126 mg/ml or an abnormal oral glucose tolerance test (post-OGTT glucose ≥200 mg/ml) or an abnormal hemoglobin A1C (≥6.5%). We also included in the definition of diabetes any use of prescription drugs for diabetes. Dyslipidemia was defined as a total cholesterol/high-density lipoprotein cholesterol level > 5 or use of a cholesterol lowering medication.

Cigarette use was defined using pack-years of smoking with a 3-level categorical variable defined as "never", "0-10" pack-years, and "10 and plus" pack-years; cigarette pack years was calculated as the number of exposure years multiplied by the average number of cigarettes smoked per day and divided by 20. Alcohol use was defined as "never", "former" or "current" based on self-report. Physical activity was assessed using the Global Physical Activity Questionnaire (GPAQ).[12] A dichotomous variable (yes/no) for physical activity was created based on whether or not the participant met the 2008 Physical Activity Guidelines for Americans.[13]

Prevalent coronary heart disease (CHD) was defined using a variable that combined ECG reports obtained at baseline that suggested the presence of possible old myocardial infarction, as well as self-reported diagnosis of angina, "heart attack" or cardiac procedures, i.e. angioplasty, stent or coronary artery bypass graft surgery.

Statistical Analysis

Student's t-test and the chi-square test (as appropriate) were used to compare values of characteristics at baseline for participants with and without PAD. We used multivariable logistic regression to assess the association between SA and PAD. Secondary analyses examined the association of PAD with other sleep variables including T90 (amount of recording time spent with an oxygen saturation less than 90%) or lowest oxygen saturation during the sleep period. All models were adjusted for age, sex, BMI, waist hip ratio, hypertension, CHD, diabetes, dyslipidemia, high sensitivity C-reactive protein (CRP) levels, smoking, alcohol use, physical activity, study site, and Hispanic/Latino background. Finally, differences between men and women and among the different Hispanic/Latino backgrounds in the observed associations were evaluated by testing the interaction with a more conservative significance level (0.01). Primary analyses were interpreted as statistically significant if p < 0.05. All analyses accounted for the complex survey design and sampling weights, were conducted by HCHS/SOL coordinating center (University of North Carolina – Chapel Hill) and performed using SAS 9.3 software (SAS Institute, Cary, NC) and SUDAAN software Release 11 (RTI International, Research Triangle Park, NC). The multi-stage sampling design and cohort

selection procedures have been described elsewhere in detail.[2] Briefly, participants were recruited from defined geographical areas selected to provide a representative sample of the target population and diversity among participants with regard to socioeconomic status and national origin or background. Of individuals who were screened and selected and who met eligibility criteria, 41.7% were enrolled, representing 16,415 persons from 9,872 households.

References

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